

REMARKS

Claims 1-13 and 15-24 are currently pending in this application. Claims 1-9 and 16-18 are withdrawn from consideration by the Examiner as allegedly being drawn to non-elected embodiments. Claim 14 was previously canceled without prejudice or disclaimer. Claim 10 is amended herein to recite, "wherein the concentration of amino acid used in the precipitation is less than or equal to 110 g/l." Support for that amendment can be found throughout the specification, *e.g.*, in Examples 1-4 on pages 9-18. Thus, no new matter has been added.

REJECTIONS UNDER 35 U.S.C. § 112

The Office maintains the rejection of claims 10-13, 15, and 19-24 under 35 U.S.C. § 112 ¶ 1 as allegedly failing to comply with the enablement requirement. Office Action at pp. 2-6. Specifically, the Office cites *Heimburger V. N. et al.*, "Factor VIII Concentrate, Highly-Purified and Heated in Solution," *Drug Res.*, 31:619-622 (1981) ("*Heimburger*") as allegedly demonstrating the unpredictability of the claimed invention. *Id.* Applicants respectfully traverse.

"There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue.' These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make

or use the invention based on the content of the disclosure.” M.P.E.P. § 2164.01(a), 8th Edition, August 2007 Revision (citing *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The Office analyzes each of these factors and concludes that the instant invention requires “undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching, and guidance presented.” Office Action at p. 4. Applicants respectfully disagree.

As the Office acknowledges, the nature of the invention (*Wands* Factor B) is a method for producing a concentrate of a factor VIII:C-containing von Willebrand factor (vWF/FVIII:C), comprising fractional precipitation using an alkali metal salt and an amino acid chosen from glycine, α - or β -alanine, α -, β -, or γ -aminobutyric acid, lysine, valine, asparagine, and glutamic acid, wherein the concentrate has an increased content of high molecular weight multimers of vWF, and a ratio of von Willebrand factor ristocetin cofactor activity (vWF:RCoF) to von Willebrand factor antigen (vWF:Ag) of greater than 1. See Office Action at pp. 2-3. The Office also agrees that the level of skill in the art (*Wands* Factor D) is high. (See Office Action at p. 4.)

However, the Office contends that the previously presented claims are broad (*Wands* Factor A) “because they refer to a process for producing a concentrate of factor VIII:C-containing von Willebrand factor (vWF/FVIII:C) wherein the concentrate has a ratio of vWF:RcoF [sic] to vWFAg of greater than 1.” (Office Action at p. 3.) Applicants respectfully disagree that the claims are broad and submit that the Office has merely analyzed one element of the previously presented claims and has failed to consider that the claims are also limited to: (1) alkali metal salts or alkaline earth metal salts; (2)

amino acids chosen from glycine, α - or β -alanine, α -, β -, or γ -aminobutyric acid, lysine, valine, asparagine, and glutamic acid; and (3) concentrates having an increased content of high molecular weight multimers of vWF. In addition, the currently amended claims are limited to concentrations of amino acids less than or equal to 110 g/l. Accordingly, Applicants respectfully submit that the scope of the claims is not overly broad.

The Office also contends that the amount of direction provided by the inventor (*Wands* Factor F) and the existence of working examples (*Wands* Factor G) are limited to “working examples 1 and 2 and Table 1 on pages 10 and 11” of the specification. (Office Action at p. 4.) Applicants respectfully disagree and submit that the Office has failed to consider the teachings of Examples 3-5 and Tables 3, 4, 6, 8, and 9 on pages 14-21 of the specification. These Examples and Tables disclose additional methods according to the invention in which the resulting concentrate has a vWF:RCoF/vWF:Ag ratio greater than 1. In total, the specification provides **ten** examples of operative embodiments of the invention. Moreover, Examples 3-5 and Tables 4, 6, 8, and 9 also disclose methods in which the vWF:RCoF/vWF:Ag ratio is less than 1. By comparing the operable and inoperable examples disclosed in the specification, one skilled in the art can readily ascertain the conditions required to produce a concentrate with a vWF:RCoF/vWF:Ag ratio greater than 1. Accordingly, Applicants respectfully submit that the specification provides sufficient working examples and direction to allow one skilled in the art to practice the instantly claimed invention.

The Office’s main argument focuses on the state of the prior art (*Wands* Factor C), the level of predictability in the art (*Wands* Factor E), and the quantity of experimentation needed to make or use the invention (*Wands* Factor H). Specifically,

the Office contends that *Heimbürger* establishes the state of the prior art and that “the instant invention is unpredictable” because *Heimbürger* “teaches that the same method steps [as the instant invention] produce a concentrate in which the ratio is less than 1.” Office Action at p. 3. Accordingly, the Office concludes that “there is a large quantity of experimentation necessary to determine whether the method claimed” is actually operable. *Id.* at p. 4. Applicants respectfully disagree.

As discussed in the Declaration of Gerhardt Kumpe Under 37 C.F.R. § 1.132 (“*Kumpe Declaration*”), one of the inventive features of the instant application is the unexpected discovery that in order to reproducibly generate a concentrate of a factor VIII:C-containing von Willebrand factor in which the ratio of von Willebrand factor ristocetin cofactor activity to von Willebrand factor antigen is greater than 1, the fractional precipitation should use concentrations of glycine less than or equal to 110 g/l. (*Kumpe Declaration* at ¶ 9.) Specifically, Examples 1-4 on pages 9-18 of the specification demonstrate that in all but one case, glycine concentrations greater than 110 g/l resulted in vWF:RCoF/vWF:Ag ratios less than 1, whereas glycine concentrations less than or equal to 110 g/l consistently resulted in ratios greater than 1. (See Exhibit A.) The *Kumpe Declaration* also establishes that the concentration of glycine used in *Heimbürger* was 128.3 g/l. (*Id.* at ¶ 8.) Thus, the vWF:RCoF/vWF:Ag ratio observed in *Heimbürger* is less than 1 and the concentration of glycine used in that reference is greater than 110 g/l. Accordingly, rather than calling the operability of the instant invention into question, in fact, *Heimbürger* supports Applicants’ discovery that glycine concentrations greater than 110 g/l do not usually produce vWF:RCoF/vWF:Ag ratios greater than 1.

Without acquiescing to the rejection and solely to facilitate prosecution, Applicants have amended the claims to recite, “wherein the concentration of amino acid used in the precipitation is less than or equal to 110 g/l.” Since *Heimbürger* uses a glycine concentration that is greater than 110 g/l (see *Kumpe Declaration* at ¶ 8), the steps of the instant invention are not the same as *Heimbürger*. Thus, the Office’s argument that “since the steps [of the instant invention and *Heimbürger*] are the same, the results must inherently be the same” is rendered moot. Office Action at p. 6.

For at least these reasons, Applicants respectfully submit that the instantly claimed invention is fully enabled by the originally filed specification. Accordingly, Applicants respectfully request that the rejection of claims 10-13, 15, and 19-24 under 35 U.S.C. § 112 ¶ 1 be withdrawn.

CONCLUSION

Applicants respectfully request that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing claims 10-13, 15, and 19-24 in condition for allowance. Applicants submit that the proposed amendment of claim 10 does not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner.

Applicants also submit that the entry of the amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.


In view of the foregoing remarks, Applicants submit that this claimed invention is neither anticipated nor rendered obvious in view of the prior art references cited against this application. Applicants therefore request the entry of this Amendment, the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: March 14, 2008

By: 
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Attachments: Declaration of Gerhardt Kumpe Under 37 C.F.R. § 1.132 with Exhibit A.